CLAIM AMENDMENT

Please amend the claims as set forth below:

1. (Currently amended) A method for introducing into a plant species the enzyme catalyzing the aryl migration of a flavanone to form an isoflavanone intermediate or an isoflavone, comprising:

introducing a DNA segment encoding said enzyme into said plant to form a transgenic plant, wherein the enzyme comprises at least about 97% amino acid identity to the polypeptide encoded by nucleotide 36 to nucleotide 1598 of SEQ ID NO: 1 and/or nucleotide 92 to nucleotide 1657 of SEQ ID NO:4, wherein said transgenic plant expresses said DNA segment under the control of a suitable constitutive or inducible promoter when said transgenic plant is exposed to conditions which permit expression.

2. (Currently amended) The method of Claim 1, wherein the plant comprises chalcone synthase, chalcone reductase, and chalcone isomerase genes that are ~~also~~ expressed to form liquiritigenin in said plant to cause in vivo formation of daidzein or a daidzein derivative.

3. (Previously presented) The method of Claim 2, wherein said plant is further transformed to comprise said chalcone synthase, chalcone reductase, and chalcone isomerase genes.

4. (Previously presented) The method of Claim 1 or 2, wherein said plant further comprises downstream genes to metabolize said formed isoflavanone intermediate or isoflavone to biologically active isoflavonoid derivatives or conjugates.

5. (Previously presented) The method of Claim 4, wherein said downstream gene is selected from the group consisting of isoflavone *O*-methyltransferase, isoflavone 2'-hydroxylase, isoflavone reductase, and vestitone reductase.

6. (Previously presented) The method of Claim 5, wherein said plant comprises downstream gene 4'-*O* methyltransferase to form biochanin A or a biochanin A derivative.

7. (Previously presented) The method of claim 1, wherein the plant is a naturally isoflavonoid-producing plant, wherein said transgenic plant expresses said DNA segment under

the control of a suitable constitutive or inducible promoter when said transgenic plant is exposed to conditions which permit expression and wherein the plant exhibits increased levels of isoflavonoid compounds from the expression.

8. (Previously presented) The method of Claim 7, wherein said isoflavonoid is selected from the group consisting of an isoflavonone intermediate, an isoflavone, an isoflavone derivative, and an isoflavone conjugate.

9. (Previously presented) The method of Claim 1, wherein said DNA segment comprises isolated genomic DNA.

10. (Previously presented) The method of Claim 1, wherein said DNA segment comprises recombinant cDNA.

11. (Currently amended) The method of Claim 1, wherein said DNA segment comprises a CYP93C gene.

12. (Currently amended) The method of Claim 11, wherein said DNA segment comprises ~~gene consists of~~ the sequence from nucleotide 36 to nucleotide 1598 of the sequence depicted in SEQ ID NO: 1.

13. (Previously presented) The method of Claim 1, said DNA segment is a *Medicago truncatula* homolog of a CYP93C gene.

14. (Currently amended) The method of Claim 11~~2~~, wherein said DNA segment comprises ~~gene consists of~~ the sequence from nucleotide 92 to nucleotide 1657 of the sequence depicted in SEQ ID NO:4.

15. (Previously presented) The method of Claim 8, wherein said flavanone is liquiritigenin.

16. (Previously presented) The method of Claim 8, wherein said flavanone is naringenin.

17. (Previously presented) The method of Claim 1, wherein said transgenic plant possesses an isoflavonoid which is isolated from said plant and used to prepare a food.

18. (Previously presented) The method of Claim 1, wherein said transgenic plant possesses an isoflavonoid which is isolated from said plant and used to prepare a food stuff, a nutritional supplement, an animal feed supplement, a nutraceutical, or a pharmaceutical.

19. (Previously presented) The method of Claim 1, wherein said transgenic plant possesses an isoflavonoid which provides a pharmaceutical benefit to a patient.

20. (Withdrawn) A method for synthesizing an isoflavanone intermediate or an isoflavone from a flavanone by expressing a recombinant CYP93C gene segment in a suitable bacterial, fungal, algal, or insect cell system.

21. (Withdrawn) A method of reducing the levels of isoflavonoid compounds in a naturally isoflavonoid-producing plant comprising introducing and expressing an antisense or gene silencing construct that contains an intact CYP93C gene or segments thereof into said plant.

22. (Withdrawn) The method of Claim 20 or 21, wherein said gene consists of the sequence from nucleotide 36 to nucleotide 1598 of the sequence depicted in SEQ ID NO:1.

23. (Withdrawn) The method of Claim 20 or 21, wherein said gene consists of the sequence from nucleotide 92 to nucleotide 1657 of the sequence depicted in SEQ ID NO:4.

24. (Withdrawn) A naturally non-isoflavonoid producing plant cell transformed by introducing a DNA a segment encoding the enzyme catalyzing the aryl migration of a flavanone to form an isoflavanone intermediate or an isoflavone, wherein said transgenic plant cell expresses said DNA segment under the control of a suitable constitutive or inducible promoter when exposed to conditions which 5 permit expression.

25. (Withdrawn) The plant cell of Claim 24, wherein chalcone synthase, chalcone reductase, and chalcone isomerase genes are also expressed in said plant to cause in vivo formation of daidzein or a daidzein derivative.

26. (Withdrawn) The plant cell of Claim 25, wherein said plant cell is further transformed to comprise said chalcone synthase, chalcone reductase, and chalcone isomerase genes.

27. (Withdrawn) The plant cell of Claim 24 or 25, wherein said plant cell further comprises downstream genes to metabolize said formed intermediate or isoflavone to biologically active isoflavonoid derivatives or conjugates.

28. (Withdrawn) The plant cell of Claim 27, wherein said downstream gene is selected from the group consisting of isoflavone *O*-methyltransferase, isoflavone 2'-hydroxylase, isoflavone reductase, and vestitone reductase.

29. (Withdrawn) The plant cell of Claim 28, methyltransferase to form biochanin A in said plant cell comprises downstream gene 4'-0-A derivative.

30. (Withdrawn) A naturally isoflavonoid-producing plant cell transformed by introducing a DNA segment encoding the enzyme catalyzing the aryl migration of a flavanone to yield an isoflavonoid to form a transformed plant cell, wherein said transformed plant cell expresses said DNA segment under the control of a suitable constitutive or inducible promoter when exposed to conditions which permit expression.

31. (Withdrawn) The plant cell of Claim 30, in said isoflavonoid is selected from the group isoflavone, an isoflavone derivative, and an consisting of an isoflavonone isoflavone conjugate.

32. (Withdrawn) The plant cell of Claim 24, 30 or 31, wherein said DNA segment comprises isolated genomic DNA.

33. (Withdrawn) The plant cell of Claim 24, 30 or 31, wherein said DNA segment comprises recombinant cDNA.

34. (Withdrawn) The plant cell of Claim 24, 30 or 31, wherein said DNA segment comprises CYP93C gene.

35. (Withdrawn) The plant cell of Claim 34, wherein said DNA segment consists of the sequence from nucleotide 36 to nucleotide 1598 of the sequence depicted in SEQ ID NO: 1.

36. (Withdrawn) The plant cell of Claim 24, 30 or 31, wherein said DNA segment is a *Medicago truncatula* homolog of a CYP93C gene.

37. (Withdrawn) The plant cell of Claim 36, wherein said gene consists of the sequence from nucleotide 92 to nucleotide 1657 of the sequence depicted in SEQ ID N0:4.

38. (Withdrawn) A transgenic plant cell having reduced levels of isoflavonoid compounds, said plant cell transformed by introducing an antisense or gene silencing construct that contains an intact CYP93C gene or segments thereof into said plant cell.

39. (Withdrawn) The plant cell of Claim 38, wherein said gene consists of the sequence from nucleotide 36 to nucleotide 1598 of the sequence depicted in SEQ ID NO: 1.

40. (Withdrawn) The plant cell of Claim 38, wherein said gene consists of the sequence from nucleotide 92 to nucleotide 1657 of the sequence depicted in SEQ ID NO:4.

41. (Withdrawn) An isolated gene or DNA segment comprising a portion which encodes a cytochrome P450 of the CYP93 family that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said portion consists of nucleotide 36 to nucleotide 1598 of the sequence depicted in SEQ ID NO: 1.

42. (Withdrawn) The gene or DNA segment of Claim 41, wherein said gene is the soybean gene encoding the enzyme catalyzing the aryl migration of liquiritigenin.

43. (Withdrawn) The gene or DNA segment of Claim 41, wherein said gene is the soybean gene encoding the enzyme catalyzing the aryl migration of naringenin.

44. (Withdrawn) A protein encoded by a portion of an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said portion consists of nucleotide 36 to nucleotide 1598 of the sequence depicted in SEQ ID NO: 1.

45. (Withdrawn) An isolated gene or DNA segment comprising a portion which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said portion is a *Medicago truncatula* homolog of a CYP93C gene.

46. (Withdrawn) The gene or DNA segment of Claim 45 consisting of nucleotide 92 to nucleotide 1657 of the sequence depicted in SEQ ID NO:4.

47. (Withdrawn) The gene or DNA segment of Claims 45 or 46, wherein said gene is the *Medicago truncatula* gene encoding the enzyme catalyzing the aryl migration of liquiritigenin.

48. (Withdrawn) The gene or DNA segment of Claims 45 or 46, wherein said gene is the *Medicago truncatula* gene encoding the enzyme catalyzing the aryl migration of naringenin.

49. (Withdrawn) A protein encoded by a portion of an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said portion is a *Medicago truncatula* homolog of a CYP93C gene.

50. (Currently amended) A transgenic plant transformed with an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein the cytochrome P450 comprises at least about 97% amino acid identity to the polypeptide encoded by nucleotide 36 to nucleotide 1598 of SEQ ID NO: 1 and/or nucleotide 92 to nucleotide 1657 of SEQ ID NO:4, wherein said transgenic plant exhibits increased levels of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said isolated gene or DNA segment.

51. (Previously presented) The transgenic plant of Claim 50, wherein the level of bacterial or fungal symbiosis is increased.

52. (Previously presented) The transgenic plant of Claim 50, wherein at least a portion of said transgenic plant is made into a composition suitable for ingestion as a food stuff, a nutritional supplement, an animal feed supplement, or a nutraceutical.

53. (Previously presented) The transgenic plant of Claim 50, wherein at least a portion of said edible transgenic plant material capable of being ingested for its nutritional value is made into a food.

54. (Currently amended) A method of preparing a nutraceutical composition for achieving a nutritional effect using a transgenic plant transformed with an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein the cytochrome P450 comprises at least about 97% amino acid identity to the polypeptide encoded by nucleotide 36 to nucleotide 1598 of SEQ ID NO: 1 and/or nucleotide 92 to nucleotide 1657 of SEQ ID NO:4, wherein said transgenic plant exhibits increased levels of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said isolated gene or DNA segment.

55. (Withdrawn) A method of preparing a pharmaceutical composition for achieving a therapeutic effect using a transgenic plant transformed with an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said transgenic plant exhibits increased levels of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said isolated gene or DNA segment.

56. (Withdrawn) A method of using a transgenic plant transformed with an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said transgenic plant exhibits increased levels of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said isolated gene or DNA segment to provide a nutraceutical benefit to a human or animal administered said isoflavonoid.

57. (Withdrawn) The method of Claim 56, wherein said isoflavonoid is administered by ingestion of at least a portion of said plant.

58. (Withdrawn) The method of Claim 56, wherein said isoflavonoid is administered by ingestion of a composition comprising an isoflavonoid isolated from said plant.

59. (Withdrawn) A method of transforming a plant with an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said transgenic plant exhibits increased

levels of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said isolated gene or DNA segment.

60. (Withdrawn) The method of Claim 59, wherein the nutritional value of said plant is increased.

61. (Withdrawn) The method of Claim 59, wherein the disease resistance in said plant is increased.

62. (Withdrawn) The method of Claim 59, wherein bacterial or fungal symbiosis in said plant is increased.

63. (Withdrawn) The method of claim 59, wherein said plant is a leguminous plant.

64. (Withdrawn) The method of claim 63, wherein the nodulation efficiency of said plant is increased.

65. (Withdrawn) A leguminous transgenic plant exhibiting increased nodulation efficiency, wherein said transgenic plant is transformed with an isolated gene or DNA segment which encodes a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said transgenic plant exhibits increased levels of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said isolated gene or DNA segment.

66. (Withdrawn) A transgenic plant comprising at least one recombinant DNA sequence encoding a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein said transgenic plant exhibits an increased level of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said recombinant DNA sequence.

67. (Currently amended) Seed from a transgenic plant comprising at least one recombinant DNA sequence encoding a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein the cytochrome P450 comprises at least about 97% amino acid identity to the polypeptide encoded by nucleotide 36 to nucleotide 1598 of SEQ ID NO: 1 and/or nucleotide 92 to nucleotide 1657 of SEQ ID NO:4, wherein the

seed comprises the recombinant DNA sequence, wherein said transgenic plant exhibits an increased level of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said recombinant DNA sequence.

68. (Currently amended) Progeny from a transgenic plant comprising at least one recombinant DNA sequence encoding a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein the cytochrome P450 comprises at least about 97% amino acid identity to the polypeptide encoded by nucleotide 36 to nucleotide 1598 of SEQ ID NO: 1 and/or nucleotide 92 to nucleotide 1657 of SEQ ID NO:4, wherein the progeny comprises the recombinant DNA sequence, wherein said transgenic plant exhibits an increased level of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said recombinant DNA sequence.

69. (Currently amended) Progeny from seed of a transgenic plant comprising at least one recombinant DNA sequence encoding a cytochrome P450 that can catalyze the aryl migration of a flavanone to yield an isoflavanone intermediate or an isoflavone, wherein the cytochrome P450 comprises at least about 97% amino acid identity to the polypeptide encoded by nucleotide 36 to nucleotide 1598 of SEQ ID NO: 1 and/or nucleotide 92 to nucleotide 1657 of SEQ ID NO:4, wherein the progeny comprises the recombinant DNA sequence, wherein said transgenic plant exhibits an increased level of an isoflavonoid when compared to the level of said isoflavonoid in plants of the same species which do not comprise said recombinant DNA sequence.

RESPONSE TO THIRD OFFICE ACTION

A. Status of the Claims

Applicants confirm the election to prosecute the Group I claims. The Examiner has agreed to examine SEQ ID NO:1 and SEQ ID NO:4 with the elected Group. Claims 1, 2, 11, 12, 14, 50, 54 and 67-69 were amended. Support for the amendment to claim 2 can be found at page 22, lines 6-23. Support for the remaining amendments can be found at page 18, line 5-22 of the PCT application publication and in claims 5 and 7.

Claims 20-49 and 55-66 have been withdrawn from consideration. Claims 1-19, 50-54 and 67-69 are within the elected group, have been examined and are presented for reconsideration.

B. Rejection of Claims Under 35 U.S.C. §112, First Paragraph – Written Description

The Action rejects claims 1-19, 50-54 and 67-69 under 35 U.S.C. §112, first paragraph as lacking an adequate written description. In particular, it is stated that Applicants have not described the genus of nucleic acids encoding an enzyme catalyzing the aryl migration of a flavanone to form and isoflavanone intermediate.

In response, Applicants note that the current claims have been amended to specify that the enzyme catalyzing the aryl migration of a flavanone to form an isoflavanone intermediate or an isoflavone comprises at least about 97% amino acid identity to the polypeptide encoded by nucleotide 36 to nucleotide 1598 of SEQ ID NO: 1 and/or nucleotide 92 to nucleotide 1657 of SEQ ID NO:4. This constitutes concrete structural information supporting a full written description of the claimed subject matter. The claims therefore recite identifiable structural features in compliance with the first paragraph of §112. *The Regents of The University of*

California v. Eli Lilly and Co., 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). It is therefore believed that the rejection is now moot and removal thereof is thus requested.

C. Rejection of Claims Under 35 U.S.C. §112, First Paragraph - Enablement

The Action rejects claims 1-19, 50-54 and 67-69 under 35 U.S.C. §112, first paragraph as not being enabled. In particular, it is asserted that the specification is enabling for production of genistein in plants that do not normally produce isoflavonoids and for increasing production of isoflavonoids in plants normally producing these compounds, but: (1) does not enable production of daidzein in plants that do not normally produce isoflavonoids using SEQ ID NO:1 or SEQ ID NO:4 or other CYP93C sequences, and (2) is not enabling for production of genistein in plants that normally produce isoflavonoids using SEQ ID NO:4 or any sequence other than SEQ ID NO:1.

In response to the assertion that production of daidzein in plants that do not normally produce isoflavonoids is not enabled, Applicants note that claim 2, the only claim under consideration reciting daidzein formation, has been amended to recite that the claimed plant expresses chalcone synthase, chalcone reductase, and chalcone isomerase to form liquiritigenin to cause in vivo formation of daidzein or a daidzein derivative. As set forth at page 22 of the application, this is all that is required for production of daidzein. Daidzein is formed from liquiritigenin. The presence of liquiritigenin results from the presence of the three genes recited in the claims: chalcone synthase, chalcone reductase, and chalcone isomerase. Therefore the scope of the claims is fully commensurate with the scope of enabled subject matter. It is therefore believed that the rejection is now moot and removal thereof is respectfully requested.

With respect to the assertion that the claims are not enabled for production of genistein in plants that normally produce isoflavonoids using SEQ ID NOs:1 or 4, Applicants direct attention to the attached Declaration of Dr. Richard Dixon (**Appendix A**). There, Dr. Dixon describes studies showing that introduction of the *M. truncatula* enzyme catalyzing the aryl migration of a flavanone to form an isoflavanone intermediate into alfalfa results in production of genistein. Alfalfa is a plant that naturally produces isoflavonoids. As explained by Dr. Dixon, the results therefore demonstrate that a plant normally producing isoflavonoids modified with an enzyme catalyzing the aryl migration of a flavanone to form an isoflavanone intermediate would in fact produce genistein.

In view of the foregoing evidence, Applicants respectfully submit that the full scope of claims has been enabled. Removal of the rejection is thus respectfully requested.

D. Rejection of Claims Under 35 U.S.C. §112, Second Paragraph

The Action rejects claim 14 under 35 U.S.C. §112, second paragraph, as being indefinite for being drawn to SEQ ID NO:4 yet depending upon claim 12 drawn to SEQ ID NO:1.

In response, Applicants note that claim 14 has been amended to correct this error. Removal of the rejection is thus respectfully requested.

E. Rejection of Claims Under 35 U.S.C. §101

The Action rejects claims 67-69 as directed to non-statutory subject matter for not specifying that the subject matter is directed to transgenic compositions. In response, Applicants note that the claims have been amended to correct this error. Removal of the rejection is thus respectfully requested.